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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/049,847	BAY ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29,30,32,38-40,42-44 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-30, 32, 38-40, 42-44 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/7/2005 has been entered.

Status of Claims

Claims 1-28, 31, 33-37, 41 and 45-46 have been cancelled.

Claims 29-30, 32, 38-40, 42-44 and 47 are under consideration and examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-30, 32, 38-40, 42-44 and 47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons advanced in the Office actions of 1/30/03 and 7/14/04.

Response to Arguments

In view of the amendments to the claims the (new matter) rejection under paragraphs A and B in the last Office action (7/14/04) has been obviated.

Claims 29-30, 32, 38-40, 42-44 and 47, as amended, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons advanced in the Office actions of 1/30/03 and 7/14/04 and reiterated below.

The specification fails to provide a written description for a vaccine or immunogenic composition in a method effective against the huge scope of tumors using the huge scope of the conjugate comprising a tumor antigen or its derivative. It is well known in the art that vaccination indicates a protective

effect. The complex nature of tumors, let alone its cure, to date remains still elusive. For some tumors, the etiologic agent that causes said tumor remains undefined. To date agents believed to have therapeutic effect against tumors are only candidates or promising leads for said therapy. Example (3) in the specification, page 27 describes protection induce by the conjugate against murine adenocarcinoma in mice. There is no correlation of the results obtained from the specific antigen as applied to the specific tumor, adenocarcinoma, to the huge scope of the tumor antigen and tumors. The claims recite for several and numerous huge scope for the undefined variables such as the tumor antigen, or its derivatives and the tumors being prevented. Note the Dalgleish reference which discloses the "numerous problems which are encountered when an anti-tumor immune response is desired". Furthermore, the specification provides only a general description of the derivative. The exemplification with respect to this derivative is nil. The description is directed to a single tumor antigen, galactosyl-N-acetyl serine. There is no description or correlation of this single tumor antigen to the huge scope of a tumor antigen or a carbohydrate derivative of the tumor antigen. To satisfy a written description requirement for a claimed genus a sufficient description of a representative number of species by actual

reduction to practice or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. A representative number of species means that the species, which are adequately described, are representative of the entire genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure indicates that the applicants have invented species sufficient to constitute the gen[us]. Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004).

Response to Arguments

Applicant's arguments filed 11/17/04 have been fully considered but they are not persuasive.

As a preliminary matter, applicants' response refer to 35 USC 112, second paragraph rejection but the arguments are drawn to the rejection under 35 USC 112, first paragraph. The responses are however treated under the first paragraph.

Applicants deem that Example 1 discloses a method for the synthesis of the Tn antigen by a completely chemical procedure. However, the completely synthetic Tn antigen is not the exact natural product that would have been extracted from the cell membrane of the tumor cell expressing the same has entirely preserved its antigenicity since it is recognized by antibodies specific to the natural Tn antigen as can be seen from Example 2. Moreover, this completely synthetic chemical Tn antigen is also immunogenic since it induces in vivo and effective antibody response that decreases the mortality of tumor bearing animals immunized therewith as can be seen from Example 3.
Any modification in the chemical synthesis of the Tn antigen is easily available to one skilled in the art as well as the possibility to check by routine procedures as disclosed in Examples 1 to 4 that the modified Tn antigen has the derivative of the Tn antigen preserves its antigenicity and immunogenicity. The essential feature of the claimed peptide-carbohydrate conjugate does not consist in the structure of the tumor carbohydrate moiety or the derivative thereof that is used but on the general structure of the conjugate which allows an effective antibody response at a level that was not reached with any of the immumogenic structures disclosed in the prior art.

In response, the claims are not drawn to a method of synthesis or to a method of making the conjugate. Rather, to a conjugate irrespective of how it is made. A review of Examples 1-4 in the specification, reveal a specific tumor antigen against a specific tumor and a single derivative of the antigen. There is nothing in the Examples (1-4) that correlate the description for the single or specific compounds to the huge scope of the claimed tumor antigen or a vaccine containing said genus claim. It is not apparent as to the kind of modification(s) that can be made on an antigen without any define structure of the antigen. Thus, synthesis becomes only routine, if the structure that is to be synthesized is given. As to applicants' assertion that the essential feature of the claimed conjugate is on the general structure of the conjugate and not on the structure of the tumor carbohydrate moiety or the derivative. Attention is drawn to LoMan reference (The Journal of Immunology, page 2851, col. 2 which state that the choice of Tn recognized by a single mab, could lead to the induction of a skewed anti-Tn immune response. Lo-Man et al (Cancer Research), page 1520, states that the fully synthetic immunogen (MAG:TnPV) is fully defined in composition and carries a high saccharidic epitope ratio over the entire molecule and that protein conjugates that present ambiguity in both composition and

structure, presents major obstacle for reproducible preparations. See also page 1521, col. 2 which shows that as simple as the attachment of the specific Tn antigen at the wrong site results in T-cell not recognizing said antigen.

With respect to the efficacy of the claimed peptide-carbohydrate conjugates for treating cancer, applicants assert that the same wi11 be efficient in preventing, treating or at least reducing the incidence of a cancer in an animal body. Applicants submit six articles to support the usefulness of the claimed peptide carbohydrate conjugates for treating cancer.

In reply, a review of these references reveals the requirement of specificity of the antigen tumor against a (specific) tumor. See specifically the above-cited Lo-Man references. In biotechnological invention one cannot necessarily claim a genus after only describing a single species because there may be unpredictability in the results obtained from species other than those specifically described. (As evident from the Lo-Man references and the references newly submitted by applicants.) Applicants may not preempt an unduly large field by the expedient of making broad prophetic statements in the specification and claim unless the accuracy of such statements is sufficiently supported by well-established principles or by sufficient number of examples.

[Reciting the specific tumor antigen described against a (specific) tumor as described in the specification will obviate this rejection.]

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, second paragraph

In view of the amendments to the claims, cancellation of some claims and applicants' arguments, the rejections under this statute have been overcome.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-30, 32, 38-40, 42-44 and 47, as amended, are rejected under 35 U.S.C. 103(a) as being obvious over Chong et

al (5,679,352) or Chong in combination with Jondal (5,807,559) for reasons set forth in the last Office action.

Response to Arguments

Applicants assert that the Chong et al patent discloses dendrimeric conjugates which combine only peptide T and B-epitopes and Chong et al does not disclose or suggest any synthetic conjugate wherein the B-epitope is included in a carbohydrate moiety. Beginning at line 65 of column 3 through line 67 of column 6, Chong et al exclusively discloses synthetic conjugates wherein B-cell epitope is only a peptide compound and particularly, one of the P1, P2 and P6 proteins from hemophilus influenza (HIV). It is clear from various portions of Chong et al particularly, line 62 of column 4 wherein B-cell epitope of the P1 protein is cited in line 8 of column 5 wherein the B-cell epitope of P2 is cited and in line 19 of column 5 wherein B-cell epitope of P6 is cited. When the PRP carbohydrate moiety is used in the dendrimeric structures of Chong et al, it is only as a carrier molecule as expressed by the term "PRP-carrier conjugate vaccine" in lines 50 to 51 of column 6. Moreover, even in the case where the PRP carbohydrate moiety included in several embodiments of the dendrimeric structures of Chong et al would induce some antibody response against PRP which is neither

described nor taught in Chong et al. It would remain that the said antibody response would not consist an antibody response against the "carbohydrate tumor antigens."

In response, Chong at col. 3, lines 15-20 recites the immunogenic synthetic conjugate comprising synthetic PRP oligomers and the antigenic determinants of Hi outer membrane protein. Chong at col. 2, lines 55-65 discloses that the synthetic PRP-peptide conjugate vaccine enhanced protective ability and T-cell priming, which would indicate that the PRP induces antibody (B-cell) responses. Thus, whether PRP is termed as a carrier is immaterial as the conjugate is known as shown by e.g., Fig. 1. Attention is drawn to Chong at col. 17, lines 27-32 which discloses that the synthetic glycoconjugate may be used to produce vaccines eliciting antibodies against proteins or oligosaccharide. Such vaccines may be used to induce immunity toward tumor cells, or to produce antitumor antibodies. It is noteworthy to cite applicants' recognition in the REMARKS of 5/3/01 that Chong et al at lines 38-43, col. 3, is concerned with the enhancement of carbohydrate immunogenicity by the use of MAP type constructions containing Hib determinant as carrier molecules for the carbohydrate moiety, more precisely, the PRP carbohydrate moiety. Applicants further recognized, col. 5, lines 29-39 that Chong encompasses the use of peptides consisting of immunodominant epitope for T-cells as PRP carriers or as autologous or heterologous B-cell epitope carriers.

Applicants assert that the Jondal teachings do not overcome the deficiencies of the Chong et al patent since Jondal is exclusively interested in raising a cyctotoxic T-cell response against a carbohydrate moiety and teaches exclusively a peptide-carbohydrate conjugate that raises a CTL response. One skilled in the art would have found absolutely no motivation to use any of the carbohydrate moieties disclosed by Jondal in the dendrimeric structures disclosed by Chong et al because he would not have foreseen that an effective antibody response might be raised against carbohydrate moieties.

In response, the disclosure of Jondal at col. 10, Table 1 supports the findings of Chong. Jondal discloses a conjugate of protein and tumor or bacterial antigen effective as anti-tumor or anti-bacterial antigen i.e., depending upon the vaccine or immunity one desires i.e., whether an antitumor or antibacterial vaccine. The important aspect of the conjugation of protein-polysaccharide conjugates is the desire to elicit both T and B cells responses. Accordingly, the teachings of Chong, alone or in combination with Jondal render the claimed invention prima facie obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 29, 30, 32 and 42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,676,946. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant broad conjugate with B define as a carbohydrate of a tumor antigen or derivative encompasses the specific conjugate of the '946 Patent.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
May 13, 2005